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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,883	01/23/2004	Michael Hensel	ICI 104 DIV	8282

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EXAMINER	
SHAHNAN SHAH, KHATOL S	
ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/763,883	HENSEL ET AL.	
	Examiner	Art Unit	
	Khatol S. Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2008 and 01 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,22,26,27,31-49,69,70 and 91-98* is/are pending in the application.

4a) Of the above claim(s) *1-16, 31-34,41-42, 69,70, and 91-98* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,26,27,35-40 and 43-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendments after final of 9/03/2008 are acknowledged. Claim 22 was amended to incorporate the elements of claim 30. Claim 30 has been cancelled.

2. Applicants' notice of appeal of 10/01/2008 is acknowledged.

3. Applicants' request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Status of Claims

4. Claims 1-16, 22, 26, 27, 31-49, 69, 70 and 91-98 are pending in this application. Claims 22, 26, 27, 35-40 and 43-49 are under consideration. Claims 1-16, 31-34, 41-42, 69, 70, and 91-98 are withdrawn as being drawn to no-elected inventions. Claims 17-21, 23-25, 28-30, 50-68, 71-90 and 99-100 have been canceled either by the recent or previous amendments.

Rejections Moot

5. Rejection of claim 30 are rejected under 35 U.S.C. 102(a) as being anticipated by Deiwick al. made in paragraph 19 of the office action mailed 04/03/2008 is moot in view of cancellation of said claim.

Rejections Withdrawn

6. Rejection of claims 22, 26, 35, 37, 38, 39, 40, 45,46 and 49 are rejected under 35 U.S.C. 102(a) as being anticipated by Deiwick al. made in paragraph 17 of the office action mailed 6/28/2007 is withdrawn. Applicant's arguments filed 9/03/2008 in regard to date of Deiwick et al. reference was persuasive.

7. Rejection of claims 22, 40 and 43 are rejected under 35 U.S.C. 103(a) made in paragraph 19 of the office action mailed 6/28/2007 is withdrawn. Applicant's arguments filed 9/03/2008 in regard to date of Deiwick et al. reference was persuasive.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 22, 26, 35-40 and 44-49 are rejected under 35 U.S.C. 103(a) as being obvious over Shea et al. (Proc. Natl. Acad. Sci. USA Vol. 93, pp. 2503-2597, March 1996) in view of Hensel et al. Molecular Microbiology vol. 24, no.1, pp. 155-167, 1997). Prior art of record, applicants' 1449.

Claims are drawn to an attenuated gram-negative cell comprising the SPI2 gene locus, wherein at least one effector (sse) gene of the SPI2 locus is inactivated, wherein said inactivation results in an attenuation/reduction of virulence compared to the wild type of said cell.

Shea et al. teach an attenuated gram-negative cell comprising the SPI2 gene locus, wherein at least one gene of the SPI2 locus is inactivated, wherein said inactivation results in an attenuation/reduction of virulence compared to the wild type of said cell. (see abstract and page 2593). Shea et al. teach Enterobactericae and *Salmonella* cell (see bacterial strains, page 2593 and figure 1, page 2594). Shea et al. et al. teach broad host range for *Salmonella* species causing disease (see page 2593). Shea et al. teach insertion mutation and insertion cassettes (see pages 2593, 2594 and fig 1). Shea et al. teach antibiotic resistance (see 2594 under results). Shea et al. teach a gene outside of SPI2 locus (see page 2595 under mapping boundaries of SPI2). Shea et al. do not explicitly teach sse genes. However, this deficiency has been overcome by the teachings of Hensel et al.

Hensel et al. teach an attenuated gram-negative cell comprising the SPI2 gene locus, wherein at least one gene of the SPI2 locus is inactivated, wherein said inactivation results in an attenuation/reduction of virulence compared to the wild type of said cell. (see abstract and page 155). Hensel et al. teach enterobactericae and

Salmonella cell (see table1 page 158). Hensel et al. teach SPI2 type III secretion genes including the effector genes or sse (see page 156 under results).

It would been *prima facie obvious* to one of ordinary skill in the art at the time the invention was made to combine the teachings of Shea et al. and Hensel et al. , an attenuated gram-negative cell comprising the SPI2, gene locus, wherein at least one sse gene of the SPI2 locus is inactivated to obtain an attenuated gram-negative cell comprising the SPI2 gene locus, wherein at least one gene of the SPI2 locus is inactivated, wherein said inactivation results in an attenuation/reduction of virulence compared to the wild type of said cell. One of skilled in the art would have been motivated by the teaching of Hensel et al. that mutations in SpI2 lead to strong reduction of virulence and certain mutations in SpI2 affect the ability of *Salmonella typhimurium* to secret SPI1 effector proteins (see summary). One of skilled in the art would have also been motivated by the teaching of Hensel et al. that mutations in SPI2 affect the expression of SPI1 genes.

10. Claims 22, 26, 27 and 43 are rejected under 35 U.S.C. 103(a) as being obvious over Hensel et al. Molecular Microbiology vol. 24, no.1, pp. 155-167, 1997) in view of Tsolis et al. (Infection and Immunity Vol. 63, No. 5, pp. 1739-1744, May 1995) and further in view of Public Health Agency of Canada, vol. 24-03 February 1, 1998. Prior art of record, applicants' 1449.

Claims are drawn to an attenuated gram-negative cell comprising the SPI2 gene locus, wherein at least one effector (sse) gene of the SPI2 locus is inactivated, wherein said inactivation results in an attenuation/reduction of virulence compared to the wild type of said cell. Claim 43 further recite an additional gene superoxide dismutase.

Hensel et al. teach an attenuated gram-negative cell comprising the SPI2 gene locus, wherein at least one gene of the SPI2 locus is inactivated, wherein said inactivation results in an attenuation/reduction of virulence compared to the wild type of said cell. (see abstract and page 155). Hensel et al. teach Enterobactericae and *Salmonella* cell (see table1 page 158). Hensel et al. teach SPI2 type III secretion genes including the effector genes or sse (see page 156 under results). Hensel et al. do not specifically teach an additional superoxide dismutase gene.

Tsolis et al. teach superoxide dismutase genes (sodA and sodB) of *Salmonella typhimurium* (see abstract and pages 1741- 1743). Tsolis et al. also teach attenuated *Salmonella typhimurium* (see page 1743). Tsolis et al. also teach the role of superoxide dismutase genes (sodA and sodB) in protection of bacteria from oxidative killing (see page 1739).

As to limitation of claim 27 Public Health Agency of Canada teach the specific isolate of Salmonella typhimurium DT 104.

It would have been *prima facie obvious* to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hensel et al. an attenuated gram-negative cell comprising the SPI2, gene locus, wherein at least one sse gene of the SPI2 locus is inactivated with the teachings of Tsolis et al. superoxide dismutase genes (sodA and sodB) of *Salmonella typhimurium* to obtain an attenuated gram-negative cell comprising the SPI2 gene locus, wherein at least one gene of the SPI2 locus is inactivated, wherein said inactivation results in an attenuation/reduction of virulence compared to the wild type of said cell.

One of skilled in the art would have been motivated by the teaching of Public Health Agency of Canada to use serotype DT 104 a multi drug resistant important isolate wherein has been found among broad host range.

One of skilled in the art would have been motivated by the teaching of Hensel et al. that mutations in SpI2 lead to strong reduction of virulence and certain mutations in SpI2 affect the ability of *Salmonella typhimurium* to secret SPI1 effector proteins (see summary). One of skilled in the art would have also been motivated by the teaching of Hensel et al. that mutations in SPI2 affect the expression of SPI1 genes.

Conclusion

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol S. Shahnan-Shah whose telephone number is (571)-272-0863. The examiner can normally be reached on Mon, Wed 12:30-6:30 pm, Thur12:30-4:30pm pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert B. Mondesi can be reached on (571)-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Khatol S Shahnan-Shah/
Examiner, Art Unit 1645
November 20, 2008

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645